Express Mail No: EV 456 919 625 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Falb et al.	Confirmation N	No.:	2738
Serial No.:	09/970,820	Art Unit:	1636	
Filed:	October 5, 2001	Examiner:	Burkhart,	Michael D.
For:	COMPOSITIONS AND METHODS FOR THE TREATMENT AND DIAGNOSIS OF CARDIOVASCULAR DISEASE	Attorney Dock	et No:	7853-0284-999
	INFORMATION DISCLOS	URE STATEM	ENT	
Commissioner for P.O. Box 1450 Alexandria, VA				
Sir:				
provided certain subject U.S. pate	dance with the duty of disclosure provi- information which the Examiner may cent application. It is requested that the ial to the examination of the application	consider materia Examiner make	l to the exa	mination of the
1. Enclosu	res accompanying this Information Disc	closure Statemen	nt are:	
1a.	A list of all patents, publications, a consideration by the office.	pplications, or o	ther inform	ation submitted for
1b.	A legible copy of:			
	Each U.S. patent application public	cation and U.S. a	nd foreign	patent;
	Each publication or that portion when	nich caused it to	be listed on	the PTO-1449;
	For each cited pending U.S. application the claims, and any drawing of the applications it to be listed on the PTO-1449	lication, or porti	on of the ap	plication which

abstracts of the non-English language publications.

2. This Information Disclosure Statement is filed under 37 C.F.R. §1.97(b):

Within three months of the filing date of a national application other than a continued prosecution application under §1.53(d);

application or PCT International Search Report.

1c.

1d.

all other information or portion which caused it to be listed on the PTO-1449.

Explanations of relevancy (ATTACHMENT 1(d), hereto) or English language

An English language copy of search report(s) from a counterpart foreign

		Within three months of the date of entry of the national stage as set forth in §1.491 in an international application;
		☐ Before the mailing of the first Office action on the merits;
		Before the mailing of a first Office action after the filing of a request for continued examination under §1.114.
3.		This Information Disclosure Statement is filed under 37 C.F.R. §1.97(c) after the period specified in 37 C.F.R §1.97(b), but before the mailing date of any of a final action under 37 C.F.R. §1.113, a notice of allowance under 37 C.F.R. §1.311 or an action that otherwise closes prosecution in the application.
		(Check either Item 3a or 3b)
	3a.	☐ The Certification Statement in Item 5 below is applicable. Accordingly, no fee is required.
	3b.	 ☑ The \$180.00 fee set forth in 37 C.F.R. §1.17(p) in accordance with 37 C.F.R. §1.97(c) is: ☐ enclosed ☑ to be charged to Jones Day Deposit Account No. 50-3013 (709181-999242).
		(Item 3b to be checked if any reference known for more than 3 months)
	_	
4.	Ш	This Information Disclosure Statement is filed under 37 C.F.R. §1.97(d) after the period specified in 37 C.F.R. §1.97(c), but on or before the date of payment of the issue fee.
	The Ce	rtification Statement in Item 5 below is applicable.
		The \$180.00 fee set forth in 37 C.F.R. §1.17(p) is:
		enclosed.
		☐ to be charged to Jones Day Deposit Account No. 50-3013
5.		Certification Statement (applicable if Item 3a or Item 4 is checked)
		(Check either Item 5a or 5b)
	5a.	In accordance with 37 C.F.R. §1.97(e)(1), it is certified that each item of information contained in this Information Disclosure Statement was first cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Information Disclosure Statement.
	5b.	Each item of information contained in this information disclosure statement was cited in a communication from a foreign patent office in a counterpart application, and the communication was not received by any individual designated in 37 C.F.R. §1.56(c) more than thirty days prior to the filing of this information disclosure statement.
	5c.	Pursuant to 37 C.F.R. §1.704(d), each item of information contained in this information disclosure statement was cited in a communication from a foreign patent office in a counterpart application, and the communication was not received by any individual designated in 37 C.F.R. §1.56(c) more than thirty days prior to the filing of this information disclosure statement.

6.	\boxtimes	This application is a continuation application under 37 C.F.R. §1.60 or §1.53(b) or (d).
		(Check appropriate Items 6a, 6b and/or 6c)
	6a.	A Petition to Withdraw from issue under 37 C.F.R. §1.313(b)(5) is concurrently filed herewith.
	6b.	Copies of publications A01-A06, A08, A11-A38, A40-A49, A51-A85, A87-A89 and A91-A113 listed on Form PTO-1449 from prior application Serial No. 09/176,330, filed on October 22, 1998 (now abandoned), of which this application claims priority under 35 U.S.C. §120, are not being submitted pursuant to 37 C.F.R. §1.98(d).
	6c.	Copies of the publications A07, A09, A10, A39, A50, A86, A90 and A114 listed on Form PTO-1449 were not previously cited in prior application Serial No. 09/176,330, filed on October 22, 1998, and are provided herewith.
7.		This is a Supplemental Information Disclosure Statement. (Check Item 7a)
	7a.	This Supplemental Information Disclosure Statement under 37 C.F.R. §1.97(f) supplements the Information Disclosure Statement filed on . A bona fide attempt was made to comply with 37 C.F.R. §1.98, but inadvertent omissions were made. These omissions have been corrected herein. Accordingly, additional time is requested so that this Supplemental Information Disclosure Statement can be considered as if properly filed on .
8.		In accordance with 37 C.F.R. §1.98, a concise explanation of what is presently understood to be the relevance of each non-English language publication is:
		(Check Item 8a, 8b, or 8c)
	8a.	satisfied because all non-English language publications were cited on the enclosed English language copy of the PCT International Search Report or the search report from a counterpart foreign application indicating the degree of relevance found by the foreign office.
	8b.	set forth in the application.
	8c.	enclosed as an attachment hereto.
9.	\boxtimes	The Commissioner is authorized to charge any additional fee required or credit any overpayment for this Information Disclosure Statement and/or Petition to Jones Day Deposit Account No. 50-3013 (709181-999242).
10.		No admission is made that the information cited in this Statement is, or is considered to be, material to patentability nor a representation that a search has been made (other than a search report of a foreign counterpart application or PCT International Search Report if submitted herewith). 37 C.F.R. §§1.97(g) and (h).
		Respectfully submitted,
Date:	April	4, 2005 Mills C. Stan 39,201
		Nikolaos George JONES DAY 222 East 41 st Street New York, New York 10017-6702 (212) 326-3939

LIST OF REFERENCES CITED BY APPLICANT (Use several sheets if necessary) ATTY DOCKET NO. 7853-0248-999 09/970,820 APPLICANT Falb et al. Filing date October 5, 2001 1636

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	A01	5,262,311	11/93	Pardee, et al.			
	A02	5,202,420	04/93	Zasloff, et al.			
	A03	5,418,162	05/95	Blakely, et al.			
	A04	5,422,262	06/95	Anderson, et al.			
	A05	5,424,187	06/95	Shor, et al.			
	A06	5,545,569	08/96	Grainger, et al.			
	A07	5,702,902	12/97	Louis Anthony Tartaglia			
	A08	5,834,248	11/98	Dean A. Falb			
	A09	5,968,770	10/99	Falb, et al.			
	A10	6,156,500	12/5/00	Dean A. Falb			
	A11	6,225,084	01/01	Falb, et al.			
	A12	6,054,558	04/00	Falb, et al.	11		

FOREIGN PATENT DOCUMENTS

 	DOCUMENT NUMBER	DATE	COUNTRY	CL	ASS	SUBCLASS	TRANSL	ATION
							YES	NO
A13	EP 0 282 899 A2	09/88	EPO					
 A14	EP 0 670 369 A2	09/95	EPO					
 A15	WO 95/23858	09/95	PCT		•			
A16	International Search Report, Application No. PCT/US97/02291	7/97	PCT					

A17	Adams et al.; Gene Bank, AC: AA350793
A18	Adams et al.; (Nature Genet. 4:256-267, 1993)
A19	Bampton, et al., 1999 "Electrophysiological Characterisation of the Denatte Gyrus in Five Inbred Strains of Mouse" Brain Research 841: 123-134
A20	W.M. Barnes, 1994, "PCR amplification of up to 35-kb DNA with high fidelity and high yield from λ bacteriophage templates", <i>Proc. Natl. Acad. Sci. USA</i> 91:2216-2220.
A21	Bartel et al., 1993, "Using the two-hybrid system to detect protein-protein interactions", Cellular Interactions in Dev. Chap.7, pp. 153-159.
A22	Bevilacqua et al., 1989, "Endothelial leukocyte adhesion molecule 1: An inducible receptor for neutrophils related to complement regulatory proteins and lectins", Science 243:1160-1165.
A23	Bevilacqua et al., 1991, "Selectins: A family of adhesion receptors", Cell 67:233.
A24	Bird et al., 1988, "Single-chain antigen-binding proteins", Science 242:423-426.
A25	Blachly-Dyson et al., 1993, "Cloning and functional expression in ueast of two human isoforms of the outer mitochondrial membrane channel, the voltage-dependent anion channel", J. Biol. Chem. 268:1835-1841.
A26	Black et al., 1994, "Raloxifene (LY139481 HCl) prevents bone loss and reduces serum cholesterol without causing uterine hypertrophy on ovariectomized rats", J. Clin. Invest. 93:63-69.
A27	Boise et al., 1993, "bcl-x, a bcl-2-Related gene that functions as a dominant regulator of apoptotic cell death", Cell 74:597-608.

	A28	Border & Noble, 1995, "Targeting TGF-ß for treatment of disease", Nature Med. 1:1000-1001.
1	A29	Cercek et al., 1990, "Induction of insulin-like growth factor I messenger RNA in rat aorta after balloon denudation", Circulation Res. 66:1755-1760.
1	A30	Charles et al., 1993, "Genomic structure, cDNA sequence, and expression of gly96, a growth factor-inducible immediate-early gene encoding a short-lived glycosylated protein", Oncogene 8:797-801.
7	A31	Chen et al., 1996, "A transcriptional partner for MAD proteins in TGF-ß signaling", Nature 383:691-696.
1	A32	Cheng et al., 1994, "Effective amplification of long targets form cloned inserts and human genomic DNA", <i>Proc. Natl. Acad. Sci. USA</i> 91:5695-5699.
1	A33	Cleary et al., 1986, "Cloning and structural analysis of cDNAs for bcl-2 and a hybrid bcl-2/Immunoglobulin transcript resulting from the t(14;18) translocation", Cell 47:19-28.
1	A34	Coffman et al., 1990, "Xotch, the Xenopus homolog of Drosophila Notch", Science 249:1438-1441.
	A35	A. Coghlan, 1995, "Gene dream fades away", New Scientist: 14-15
1	A36	Cybulsky & Gimbrone, 1991, "Endothelial expression of a mononuclear leukocyte adhesion molecule during atherogenesis", <i>Science</i> 251 :788-791.
1	A37	Davies et al., 1986, "Turbulent fluid shear stress induces vascular endothelial cell turnover in vitro", Proc. Natl. Acad. Sci. USA 83:2114-2117.
1	A38	Diamond et al., 1993, "Novel delayed-early and highly insulin-induced growth response genes", J. Biol. Chem. 268:15185-15192.
1	A39	Ebert, et al., 1991, "Transgenic Production of a Variant of Human Tissue-Type Plaminogen Activator in Goat Milk: Generation of Transgenic Goats and Analysis of Expression" Biotechnology, 9:835-838. (Exhibit D)
1	A40	Eppert et al., 1996, "MADR2 maps to 18q21 and encodes a TGFB-regulated MAD-related protein that is functionally mutated in colorectal carcinoma", Cell 86:543-552.
1	A41	Farrow et al., 1995, "Cloning of bcl-2 homologue by interaction with adenovirus E1B 19K", Nature 374:731-733.
,	A42	Galvin et al., 2000 "A Role for SMAD6 in Development and Homeostasis of the Cardiovascular System" Nature Genetics, 24:171-174.
	A43	M.A. Gimbrone, 1976, "Culture of vascular endothelium" <i>Progress in Hemostasis and Thrombosis</i> Grune & Stratton Inc., NY, 3:1-28.
1	A44	Grainger et al., 1995, "Tamoxifen elevates transforming growth factor-\u00df and suppresses diet-induced formation of lipid lesions in mouse aorta", <i>Nature Med.</i> 1:1067-1073.
1	A45	Grainger et al., 1993, "Proliferation of human smooth muscle cells promoted by lipoprotein(a)", Science 260:1655-1658.
1	A46	Gromadzinska & Sklodowska, 1990, "Erythrocyte glutathione peroxidase and myocardial infarction", JAMA 263:949-950.
1	A47	Guidi et al., 1986, "Platelet glutathione peroxidase activity is impaired in patients with coronary heart disease", J. Clin. Lab Invest. 46:549-551.
1	A48	Gura, T., 1995, "Estrogen: Key player in heart disease among women", Science 269:771-773.
1	A49	Hakes & Berezney, 1991, "Molecular cloning of matrix F/G: A DNA binding protein of the nuclear matrix that contains putative zinc finger motifs", <i>Proc. Natl. Acad. Sci. USA</i> 88:6186-6190.
1	A50	Hammer, et al., 1986, "Genetic Engineering of Mammalian Embryos" J. Anim. Sci. 63: 269-278
1	A51	Harrison et al.; "Molecular cloning of a novel rat G-protein-coupled receptor gene expressed prominently in lung, adrenal, and liver" (FEBS Lett. 318, 1:17-22, 1993)
1	A52	K. Heckl, 1988, "Isolation of cNDAs encoding human manganese superoxide dismutase", Nucl. Acids Res. 16:6224.
1	A53	Hochman et al., 1995, "Dissociation of synchronization and excitability in furosemide blockage of epileptiform activity", Science 270:99-102.
1	A54	Hockenbery et al., 1993, "Bcl-2 functions in an antioxidant pathway to prevent apoptosis", Cell 75:241-251.
1	A55	Hoodless et al., 1996, "MADR1, a MAD-related protein that functions in BMP2 signaling pathways", Cell 85:489-500.
1	A56	Jones et al., 1993, "Molecular cloning of human prostaglandin endoperoxide synthase type II and demonstration of expression in response to cytokines", J. Biol. Chem. 268:9049-9054.
A	A57	Kanai et al., 1995, "Identification and characterization of a prostaglandin transporter", Science 268:866-869.
I I	A58	Kita et al., 1987, "Probucol prevents the progression of atherosclerosis in Watanabe heritable hyperlipidemic rabbit, an animal model for familial hypercholesterolemia", <i>Proc. Natl. Acad. Sci. USA</i> 84:5928-5931.
I I	A59	Kojima et al., 1991, "Lipoprotein (a) inhibits the generation of transforming growth factor β: An endogenous inhibitor of smooth muscle cell migration", J. Cell Biol. 113:1439-1445.
I I	A60	Kok et al., 1989, "Decreased selenium levels in acute myocardial infarction", JAMA 261:1161-1164.

A61	Kumar & Chambon, 1988, "The estrogen receptor binds tightly to its responsive element as a ligand-induced
A62	homodimer", Cell 55:145-156. Kume et al., 1992, "Lysophosphatidylcholine, a component of atherogenic lipoprotein, induces mononuclear
AUZ	leukocyte adhesion molecules in cultured human and rabbit arterial endothelial cells", J. Clin. Invest. 90:1138-1144.
A63	F. Ledley, 1995, "Nonviral gene therapy: The promise of genes as pharmaceutical products", <i>Human Gene Therapy</i> 6:1129-1144.
A64	Li et al., 1991, "Early induction of an atherosclerosis-associated endothelial-leukocyte adhesion molecule (athero-ELAM) by an atherogenic diet in rabbits", <i>Arterioscler. Thromb.</i> 11:1397a.
A65	Leiw et al., Gene Bank (AN:T20268, D345F Homo sapiens cDNA clone D345, Nov. 28, 1994)
A66	Leiw et al., "A catalogue of genes in the cardiovascular system as identified by expressed sequence tags" 1994, PNAS, 91:10645-10649
A67	Luscinskas et al., 1989, "Endothelial-Leukocyte adhesion molecule-1-dependent and leukocyte (CD11/CD18)-dependent mechanisms contribute to polymorphonuclear leukocyte adhesion to cytokine-activated human vascular endothelium", <i>J. Immunol.</i> 142:2257-2263.
A68	Majesky et al., 1990, "PDGF ligand and receptor gene expression during repair of arterial injury", J. Cell Biol. 111:2149-2158.
A69	Malden et al., 1991, "The influence of oxidatively modified low density lipoproteins on expression of platelet-derived growth factor by human monocyte-derived macrophages", J. Biol. Chem. 266:13901-13907.
A70	E. Marshall, 1995, "Less hype, more biology needed for gene therapy",
A71	E. Marshall, 1995, "Gene therapy's growing pains", Science 269:1050-1055.
A72	Mullins, et al., 1996, "Perspectives Series: Molecular Medicine in Genetically Engineered Animals" J, Clin Invest., 98(11):S37-S40.
A73	Nagel et al., 1994, "Shear stress selectively upregualtes intercellular adhesion molecule-1 expression in cultured human vascular endothelial cells", J. Clin. Invest. 94:885-891.
A74	Navab et al., 1988, "Monocyte migration into the subendothelial space of a coculture of adult human aortic endothelial and smooth muscle cells", <i>J. Clin. Invest.</i> 82:1853-1863.
A75	Ngo, et al., 1994, "Computational Complexity, Protein Structure Prediction, and the Levinthal Paradox" The Protein Folding Problem and Tertiary Structure Prediction, K Mertz, Jr. and S. Le Grand, Editors, Birkhauser Boston Chapter 14: 491-495.
A76	Nikol et al., 1992, "Expression of transforming growth factor-\$1 is increased in human vascular restenosis lesions", J. Clin. Invest. 90:1582-1592.
A77	Ohno et al., 1994, "Gene therapy for vascular smooth muscle cell proliferation after arterial injury", Science 265:781-784.
A78	Oltvai et al., 1993, "Bcl-2 heterodimerizes in vivo with a conserved homolog, bax, that accelerates programed cell death", Cell 74:609-619.
A79	Orkin & Motulsky, 1995, "Report and recommendations of the panel to assess the NIH investment in research on gene therapy", NIH Report.
A80	Osborn et al., 1989, "Direct expression cloning of vascular cell adhesion molecule 1, a cytokine-induced endothelial protein that binds to lymphocytes", <i>Cell</i> 59:1203-1211.
A81	Patrick Jr., et al., 1995, "Shear stress and cyclic strain moduclation of gene expression in vascular endothelial cells", Blood Purification 13:112-124.
A82	Plump et al., 1992, "Severe hypercholesterolemia and atherosclerosis in apolipoprotein e-deficient mice created by homologous recombination in ES cells", <i>Cell</i> 71:343-353.
A83	Porter et al., 1992, "Plasma, platelet and erythrocyte glutathione peroxidase as risk factors in ischaemic heart disease in man", Clinical Science 83:343-345.
A84	Poston et al., 1992, "Expression of intercellular adhesion molecule-1 in atherosclerotic plaques", Am. J. Pathol. 140:665-673.
A85	Puolakkainen et al., 1993, "Serological response to <i>Chlamydia pneumoniae</i> in adults with coronary arterial fatty streaks and fibrolipid plaques", <i>J. of Clinical Microbiol.</i> 31:2212-2214.
A86	Pursel, et al., 1990, "Integration, Expression and Germ-Line Transmission of Growth Related Genes in Pigs" J,
A87	Reprod. Fert. Suppl., 41:77-87. (Exhibit B) Raftery et al., 1988, "Genetic screens to identify elements of the decapentaplegic signaling pathway in Drosophila", Genetics 139:241-254.
A88	Rapacz et al., 1986, "Lipoprotein mutations in pigs are associated with elevated plasma cholesterol and atherosclerosis", Science 234:1573-1577.
A89	Resnick et al., 1993, "Platelet-derived growth factor B chain promoter contains a cis-acting fluid shear-stress-responsive element", <i>Proc. Natl. Acad. Sci. USA</i> 90:4591-4595.
A90	Rexroad, et al., 1991, "Transferrin and Albumin-Directed Expression of Growth-Related Peptides in Transgenic
A91	Sheep" J, Animal Sci., 69:2995-3004. (Exhibit C) R. Ross, 1993, "The pathogenesis of atherosclerosis: Perspective for the 1990s", Nature 362:801-809.
I	Sambrook et al.(eds), 1989, "Estimating the Effects of Mismatches", Molecular Cloning - A Laboratory Manual 2 nd

A	Sekelsky et al., 1995, "Genetic characterization and cloning of mothers against dpp, a gene required for
	decapentaplegic function in Drosophila melanogaster", Genetics 139:1347-1358.
A	Serra & Moses, 1996, "Tumor suppressor genes in the TGF-ß signaling pathway?", Nature Med. 2:390-391.
A	Shreeniwas et al., 1991, "Reoxygenation stimulates IL-1α production, increasing leukocyte adherence to
' '	endothelium via expression of ICAM-1 and ELAM-1", Arterioscler. Council Abstracts 11:1397a.
A	Shyy et al., 1995, "Multiple cis-elements mediate shear stress-induced gene expression", <i>J. Biomechanics</i> 28 :1451-1457.
A	Simmons et al., 1988, "ICAM, an adhesion ligand of LFA-1, is homologous to neural cell adhesion molecule NCAM", <i>Nature</i> 331:624-627.
A	Speir et al., 1994, "Potential role of human cytomegalovirus and p53 interaction in coronary restenosis", <i>Science</i> 265:391-394.
A	Shreeniwas et al., 1991, "Reoxygenation stimulates IL-1α production, increasing leukocyte adherence to endothelium via expression of ICAM-1 and ELAM-1", Arterioscler. Council Abstracts 11:1397a.
A	Sigmund, 2000, "Viewpoint: Are Studies in Genetically Altered Mice Out of Control" Arteriscler Thromb. Vasc Biol., 20:1425-1429
A	Takahashi et al., 1990, "Primary structure of human plasma glutathione peroxidase deduced from cDNA sequences", <i>J. Biochem.</i> 108:145-148.
A	Takayama et al., 1995, "Cloning and functional analysis of BAG-1: A novel Bcl-2-Binding protein with anti-cell death activity", Cell 80:279-284.
A	Tanaka et al., 1993, "Sustained activation of vascular cells and leukocytes in the rabbit aorta after balloon injury", Circulation 88:1788-1803.
A	Tsujmoto et al., 1984, "Cloning of the chromosome breakpoint of neoplastic B cells with the t(14;18) chromosome translocation", <i>Science</i> 226:1097-1099.
A	The WashU-Merck EST Project (Published June 27, 1995, AN: H12679, Gene Bank)
A	Wallace & Miyada, 1987, "Oligonucleotide probes for the screening of recombinant DNA libraries", <i>Methods in Enzymology</i> 152 :432-443.
A	Wieser et al., 1995, "GS domain mutation that constitutively activate TBR-I, the downstream signaling component in the TGF-B receptor complex", EMBO J. 14:2199-2208.
A	Wilson et al., 1994, "2.2 Mb of contiguous nucleotide ssequence from chromosome III of <i>C. elegans</i> ", <i>Nature</i> 368 :32-38.
A	Wrana et al., 1994, "Mechanism of activation of the TGF-ß receptor", Nature 370:341-347.
	Weatherall, D.J., 1995, "Scope and limitations of gene therapy", British Medic
	Wang et al., 1981, "Selenium and myocardial infarction: Glutathione peroxidase in platelets", Klin. Wochenschr. 59:817-818.
A	Xu et al., 1994, "Molecular cloning and functional expression of the bumetanide-sensitive Na-K-Cl cotransporter", Proc. Natl. Acad. Sci. USA 91:2201-2205.
	Yoshimura et al., 1994, "The human plasma glutathione peroxidase-encoding gene: organization, sequence and localization to chromosome 5q32", Gene 145:293-297.
A	Owman et al., 1996, "Cloning of Human cDNA Encoding a Novel Heptahelix Receptor Expressed in Burkitt's Lymphoma and Widely Distributed in Brain and Peripheral Tissues", Biochemical and Biophysical Research Communications 288:285-292.
L	Communications 200-207-272.

EXAMINER DATE CONSIDERED

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.